AMENDMENTS TO THE DRAWINGS

The attached drawing sheets include changes to Table 1. Applicants submit with this Amendment an annotated sheet showing the changes to Table 1, and a Replacement sheet. The changes to Table 1 include adding sequence identifiers after each nucleotide sequence listed therein.

Attachment: Replacement Sheet
Annotated Sheet Showing Changes

REMARKS

Claims 1-18 are pending in this application. Claims 8-12 and 15-18 have been withdrawn as directed to non-elected subject matter. Applicants have amended claim 1 to recite that the compound is a cytokine that adjusts the intrinsic strain of the cell by modulating a cytoskeletal gene. This limitation was originally presented in claim 13, and accordingly has been deleted from claim 13. Applicants have also cancelled non-elected claims 8-12 and 15-18.

Claim 1 has been further amended to recite the additional step of culturing the cell on a substrate or in a medium. Support for this additional step can be found in the above-captioned specification, as published, at, for example, ¶¶ [0113] and [0122] (U.S. Published Pat. App. No. 2007/0077653). Claims 1-3 and 6 have been amended to replace "cells" with "cell". Claim 5 has been amended to delete the recitation of "at the beginning" of cell culturing. Claim 14 has been amended to correct a typographical error. New claims 19 and 20 are directed to specific embodiments relating to the genes or recite that the compound is IL-1β. These limitations were originally in claims 13 or 14 . As such, no new matter has been added by these amendments.

OBJECTION TO SPECIFICATION REGARDING NUCLEOTIDE SEQUENCES

The specification, particularly Table 1, has been objected to for failing to comply with 37 C.F.R. § 1.821(a)(1) and (2). Applicants have amended Table 1 to include sequence identifiers and have also submitted a Sequence Amendment. Accordingly, withdrawal of this rejection is respectfully requested.

REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 4 and 7 stand rejected under 35 U.S.C. § 112, second paragraph, for containing trademarks. The trademarks have been deleted from these claims.

Claim 14 stands rejected under 35 U.S.C. § 112, second paragraph, for a typographical error regarding "TGF-α". This typographical error has been corrected to "TNF-α".

Accordingly, withdrawal of these rejections is respectfully requested.

REJECTION UNDER 35 U.S.C. § 102

Claims 1, 13 and 14 stand rejected under 35 U.S.C. § 102 as being anticipated by Hartwig *et al.*, "Regulation of hematopoietic growth factor production by genetically modified human bone marrow stromal cells expressing interleukin-1β antisense RNA," J. OF INTERFERON AND CYTOKINE RESEARCH (2001) 21:851-860 ("Hartwig"). Hartwig discloses a study designed to examine the role of IL-1β on the expression of endogenous growth factors (Hartwig at p. 852). The study was done by generating transfectants deficient for expression of endogenous IL-1β (Hartwig at p. 852). It only reviewed the effect of reduced expression of endogenous IL-1β in HuIL-1β AS RNA transfectants (Hartwig at p. 855).

Hartwig's experiments did not administer IL-1β or any other compound that modulates an organization of a cytoskeleton of the cell and resets the intrinsic strain of the cell, and did not administer IL-1β to the transfectants. Furthermore, Hartwig does not teach or suggest that IL-1β or any of the other recited compounds is useful for manipulating an intrinsic strain of a cell or modulating an organization of a cytoskeleton of the cell, as recited in claim 1. It only linked IL-1β to growth factors and adhesion molecules (Hartwig at p. 851), not cytoskeletal proteins. Finally, Hartwig also does not teach or suggest that IL-1β or any of the other recited compounds can be administered after the cell has been cultured to reset the intrinsic strain of the cell. Instead, Hartwig teaches that IL-1β "plays an important role in regulating cytokine production" and its role in malignant hematopoiesis (Hartwig at p. 858). For these reasons, Hartwig does not teach or suggest each and every element recited in claim 1 or claims

13 and 14, which directly or indirectly depend from claim 1.

Claims 1, 6 and 7 stand rejected under 35 U.S.C. § 102 as being anticipated by United States Patent No. 6,472,202 to Banes *et al.* ("Banes"). Banes discloses a cell culture plate with a flexible cell culture membrane wells used to apply mechanical strain on a cell (Banes at col. 2, lines 25-32). Banes teaches seeding cells to a polyester foam (Banes at col. 7, lines 42-49). Bane's polyester foam is only a substrate that the cell adheres to (Banes at col. 7, lines 56-60).

On November 21, 2008, Applicants provisionally elected Group IV (claims 13 and 14) with traverse. The Examiner did not find the traversal persuasive, and therefore examined the claims as if they recited that the compound is a cytokine (Office Action at pages 2-3). Polyester foam is not a cytokine. Therefore, unless the Examiner wishes to withdraw the restriction, this rejection should be withdrawn.

Notwithstanding this, Banes does not teach or suggest that the polyester foam modulates an organization of a cytoskeleton of the cell and resets the intrinsic strain of the cell. There is no suggestion in Banes that the polyester foam has any effect on the intrinsic strain or expression of a cytoskeletal gene. Instead, one of ordinary skill would understand Banes's polyester foam as being a physical structure that imparts no biologic effect because one would not reasonably expect for the polymer to be capable of being transported across the cellular membrane. For these reasons, Banes does not teach or suggest each and every element recited in claim 1 or claims 6 and 7, which directly or indirectly depend from claim 1.

Claims 1-5 stand rejected under 35 U.S.C. § 102 as anticipated by United States Patent No. 5,912,234 to Ruoslahti *et al.* ("Ruoslahti"). Ruoslahti teaches that peptides that include a DGR(AHA), NGR(AHA) or CRGDC amino acid sequence will bind to $\alpha_5\beta_1$ intergin (Ruoslahti at col. 2, lines 32-53). As mentioned above, due to the restriction, only claims directed to cytokines have been examined. Thus, in order to establish that Ruoslahti teaches that a cytokine binds to a $\alpha_5\beta_1$ intergin, the Examiner must establish that the cytokine has one of the amino acid sequences taught by Ruoslahti. This has not been established. Moreover, the

undersigned has downloaded and searched the following IL-1β sequence from http://www.genecards.org/cgi-bin/carddisp.pl?gene=IL1B:

MAEVPELASEMMAYYSGNEDDLFFEADGPKQMKCSFQDLDLCPLDGGIQ
LRISDHHYSKGFRQAASVVVAMDKLRKMLVPCPQTFQENDLSTFFPFIFE
EEPIFFDTWDNEAYVHDAPVRSLNCTLRDSQQKSLVMSGPYELKALHLQ
GQDMEQQVVFSSFVQGEESNDKIPVALGLKEKNLYLSCVLKDDKPTLQL
ESVDPKNYPKKKMEKRFVFNKIEINNKLEFESAQFPNWYISTSQAENMPV
FLGGTKGGQDITDFTMQFVSS

From searching this sequence, the undersigned did not find an amino sequence that would bind to an $\alpha_5\beta_1$ intergin as taught by Ruoslahti. Thus, at a minimum, Ruoslahti does not teach that IL-1β binds to $\alpha_5\beta_1$ intergin, let alone any other cytokine.

Furthermore, Ruoslahti does not teach or suggest compounds that are useful in manipulating an intrinsic strain of a cell. New uses of old products or processes are patentable subject matter. In this case, Ruoslahti does not inherently teach that compounds that bind to $\alpha_5\beta_1$ intergin reset the intrinsic strain of a cell, as recited in claim 1, because there is no indication that resetting the intrinsic strain of the cell is necessary to practice Ruoslahti's invention. Ruoslahti's invention is directed to using compounds that bind to $\alpha_5\beta_1$ intergin to modulate and manipulate the cell migration (Ruoslahti at col. 1, lines 52-55). Cell migration is different from intrinsic strain of the cell because the former relates to cells moving and the latter relates to a cell's shape.

Accordingly, Ruoslahti also does not teach or suggest the invention as recited in claim 1, or claims 2-5, which directly or indirectly depend from claim 1.

Applicants also believe that new claims 19 and 20 are allowable over the cited references. Claims 19 and 20 depend from claim 1, and therefore are patentable over the cited references for the same reasons claim 1 is patentable.

CONCLUSION

In view of the amendments to the claims and remarks, Applicants respectfully request that the rejections asserted against the claims and the objections asserted against the specification be reconsidered and withdrawn, and that claims 1-7, 13, 14, 19 and 20 be allowed. Since claims 1 and 13 are broader than the elected species (IL-1β) and are believed to be in condition for allowance, rejoinder of the other non-elected cytokine species is also respectfully requested.

Respectfully submitted,

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TABLE 1. PCR CONDITIONS USED FOR EACH GENE

Gene	Primer Sequence		Product Length (bp)	Cycle Conditions	Cycles
Collagen I	5'-GGTCCTCAGGGTCTTCTTGG-3' 3'-CACCAGGAGCACCGTTGACT-5'	SEQ ID NO: 1 SEQ ID NO: 2	184	94°C, 5 min 94°C, 1 min; 45°C, 1 min; 72°C, 30 s 72°C, 5 min	28
Collagen III	5'-AGGTGAACGTGGTCCACAAGGT-3' 3'-GCACCAGCTGGTCCAGTCTCT-5'	SEQ ID NO: 3 SEQ ID NO: 4	300	94°C, 5 min 94°C, 1 min; 65°C, 1 min; 72°C, 5 min 72°C, 5 min	26
Collagen XII	5'-AGTATCAGTCTGGGCCTGGCAA-3' 3'-TTTCTCCCTCTCCAGAAAGGGCTT-5'	SEQ ID NO: 5 SEQ ID NO: 6	300	94°C, 5 min 94°C, 1 min; 65°C, 1 min; 72°C, 1 min 72°C, 5 min	35
Decorin	5'-CATCCCTTACTGAGCTTCACCTT-3' 3'-ACTCACACCAGAATAGGTTGCCTG-5'	SEQ ID NO: 7 SEQ ID NO: 8	300	94°C, 5 min 94°C, 1 min; 65°C, 1 min; 72°C, 1 min 72°C, 5 min	22
Tenascin	5'-TGTCTACAACATCAAGCTGCCTGT-3' 3'-AGCCTGCCTTACCTTCTGCTGT-5'	SEQ ID NO: 9 SEQ ID NO: 10	298	94°C, 5 min 94°C, 1 min; 65°C, 1 min; 72°C, 1 min 72°C, 5 min	37
Prolyl-hydroxylase	5'-AACAGCCAATGAAGTAGAGGCAGT-3' 3'-ACGACAATGCGTTGGGTTACTCA-5'	SEQ ID NO: 11 SEQ ID NO: 12	300	94°C, 5 min 94°C, 1 min; 60°C, 1 min; 72°C, 1 min 72°C, 5 min	22
β-Actin	5'-GCCATCCTGCGTCTGGACCGGGCT-3' 3'-GTGATGACCTGGCCGTCAGGCAGC-5'	SEQ ID NO: 13 SEQ ID NO: 14	227	94°C, 5 min 94°C, 1 min; 60°C, 1 min; 72°C, 30 s 72°C, 5 min	20